Chemistry of Heterocyclic Compounds, Vol. 38, No. 1, 2002

SYNTHESIS OF FUNCTIONALLY-SUBSTITUTED PYRROLOTHIAZOLIDINES FROM PYRROLE-2-CARBODITHIOATES, CH-ACIDS, AND HALOACETYLENES*

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Functionally substituted pyrrolothiazolidines have been synthesized by the sequential treatment of pyrrole-2-carbodithioates with methylene-reactive nitriles and haloacetylenes in a KOH–DMSO system.

Keywords: haloacetylenes, CH-acids, pyrrole-2-carbodithioates, pyrrolothiazolidines, thiazines, halogenophilic attack, nucleophilic addition.

Compounds of the thiazole series are of interest in connection with their high pharmacological activity. Products based on them include certain diuretics, anthelmintic and antihistaminic drugs [1], compounds possessing antimicrobial activity, such as sulfathiazole [2], mitodepressants and mitostatics [3], and antiparasitic, antipyretic [4], and antiviral preparations [3]. Thiazoles are used as antioxidants and vulcalization accelerators [3], photochromic compounds and chromophores [4], dyestuffs [4-6], and also in the manufacture of polymers [3-5].

We showed previously in [7-12] that the range of application of pyrrole-2-carbodithioates **1a-d** in fine organic synthesis may be broadened significantly due to their ability to react with CH-acids with the formation of functionally substituted 2-vinylpyrroles, which are key intermediates in the synthesis of annelated heterocycles.

With the aim of extending information on the reactivity of functionally substituted 2-vinylpyrroles and also of synthesizing from them new heterocyclic systems, potentially with photochromic properties and biological activity [1-6], we investigated the interaction of 1-(2-pyrrolyl)vinylthiolates **2a-d**, **3a-d**, generated *in situ* from pyrrole-2-carbodithioates **1a-d** and the methylene-reactive nitriles **4a,b** in KOH–DMSO, with 2-benzoyl-1-bromoacetylene (**5a**), 1-chloro-2-ethylthioacetylene (**5b**), and 2-(1-iodo-2-propynoxy)-1-methoxyethane (**5c**).

* Dedicated to Academician of the Russian Academy of Sciences M. G. Voronkov on his 80th birthday.

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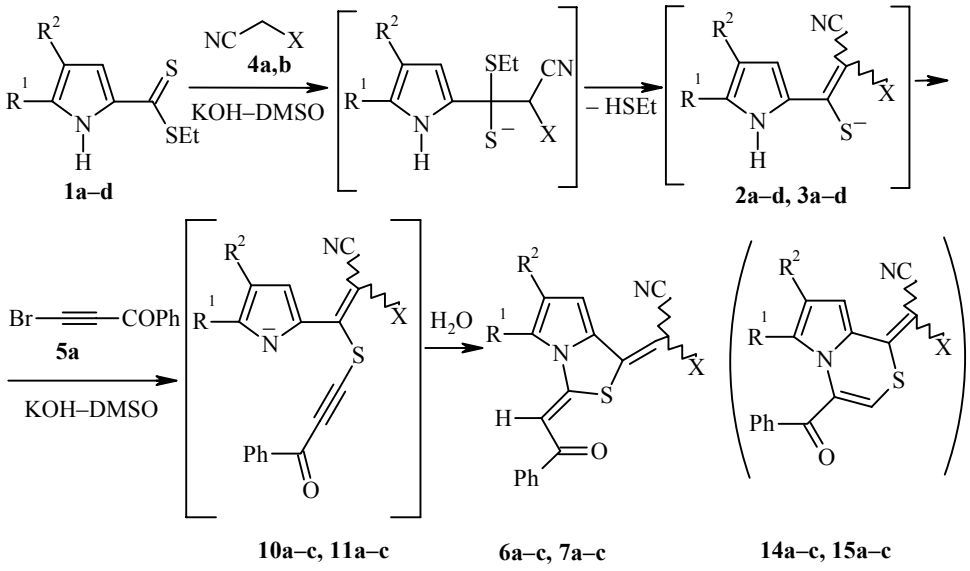
 0009-3122/02/3801-0086$27.00

The preparation of various products might be expected due to the bidentate nature of the nucleophiles (enethiolates **2**, **3**) and the presence in the haloacetylene molecule **5** of several electrophilic centers (halogen atom, C_α and C_β, and also a carbonyl group in acetylene **5a**). However compounds **2a-d** and **3a-d** reacted readily with haloacetylenes **5a** or **5b** forming the functionally substituted pyrrolothiazolidines **6a-c**, **7a-c**, **8a,d**, and **9a,d** in 37-85% yield (Schemes 1 and 2).

Scheme 1



1–3, 6, 7, 10, 11, 14 a $R^1 = R^2 = Me$, **b** $R^1 = Pr$, $R^2 = Et$, **c** $R^1 = Bu$, $R^2 = Pr$, **d** $R^1 + R^2 = (CH_2)_4$;
2, 4a, 6, 14 X = CN; **3, 4b, 7, 15** X = $CONH_2$

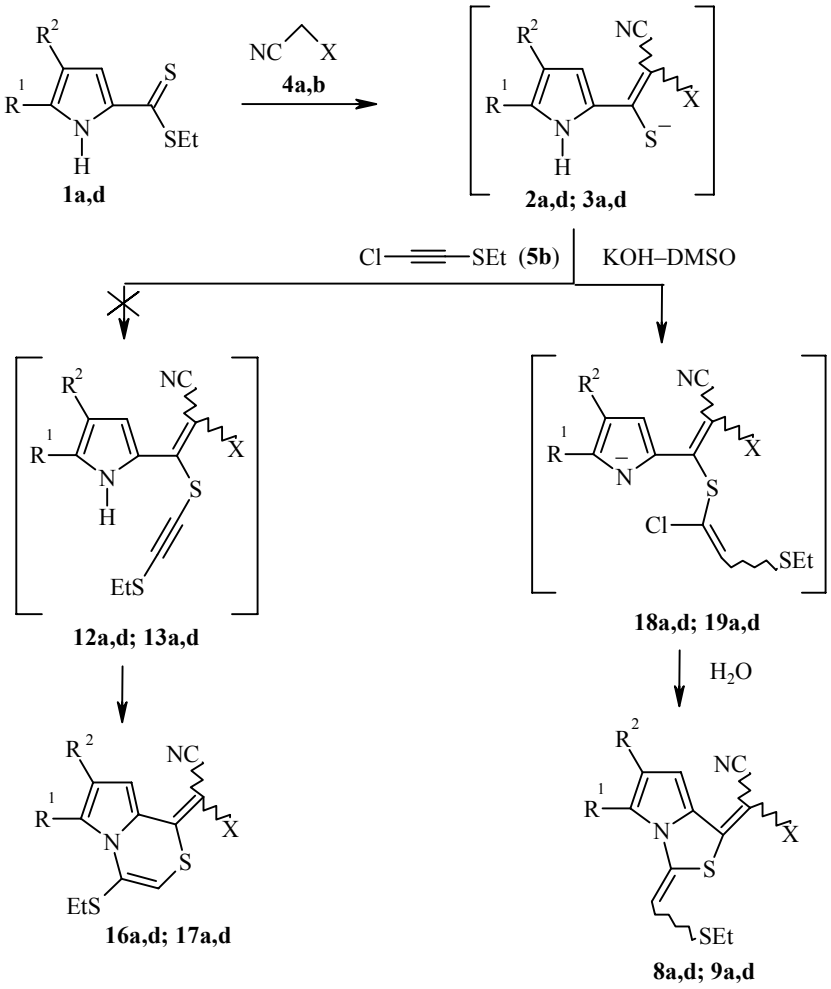
The process was effected by heating (100-110°C, 1.5 h) pyrrole-2-carbodithioates **1a-d** with anions of CH-acids generated from malononitrile **4a** or cyanoacetamide **4b** in KOH–DMSO (room temperature, 0.5 h). Subsequent interaction of the resulting enethiolates **2a-d**, **3a-d** with haloacetylenes **5a,b** occurred at room temperature.

All five stages of the synthesis of pyrrolothiazolidines **6-9** (ionization of the CH-acid, addition of the carbanion to the dithioate group of the pyrroles, elimination of ethanethiol, nucleophilic substitution of the halogen at the C_{sp} atom in the haloacetylene **5a** with enethiolates according to Scheme 1 or addition of the latter to the triple bond of the haloacetylene **5b** according to Scheme 2, and intramolecular cyclization of ethynyl sulfides **10-13** or chloroethenes **18**, **19**) were effected in one reactor without isolating the intermediate products. Under the conditions indicated the vinyl thiolates **2d**, **3d** did not react in practice with iodoacetylene **5c**, 50-60% of compound **5c** put into the reaction was recovered unchanged.

It is known that nucleophilic substitution of halogen on an acetylenic carbon atom may proceed as an addition–elimination [13,14] or is started by a halogenophilic attack [13,15]. Taking into consideration the bulk of thiolate anions **2, 3** and their increased polarizability (the presence of conjugation with the pyrrole ring and the functional groups), and also the fact that the bromine atom is a softer nucleophilic center than the *sp*-carbon, a direct halogenophilic attack is most probable in the case of bromoacetylene **5a**, leading directly to the benzoylethynyl sulfides **10-11**. Intramolecular cyclization of the latter, by addition of the NH group to the electron-deficient β-carbon atom of the triple bond, leads to the formation of products **6, 7**, having the (*Z*)-configuration. This does not tally with the expected synchronous *trans* addition [13] of the pyrrole NH

function to the triple bond of the ethynylbenzoyl group, which must have led to an (*E*)-disposition of the benzoyl group and the sulfur atom. Steric hindrance to the formation of the (*E*)-isomer may be the probable reason for the observed stereospecificity of the reaction in the present case.

Scheme 2

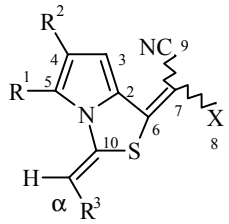


8, 9, 12–19 a $R^1 = R^2$ =Me, **d** $R^1 = R^2 = (CH_2)_4$; **8, 12, 16, 18** X = CN; **9, 13, 17, 19** X = $CONH_2$

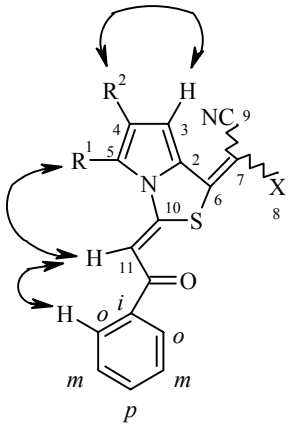
However the presence of an electronegative sulfur atom beside the triple bond, able to distribute the negative charge to a vacant orbital [16], may also assist addition of the NH group to the α- not β-carbon atom of the triple bond with the formation of thiazines **14** and **15**. A similar addition of NH group to an activated triple bond was observed in the reaction of acetylene **5** with N,N'-disubstituted thioureas [17].

A choice between the alternative structures **6**, **7** and **14**, **15** was made on the basis of data of ^{1}H and ^{13}C NMR spectroscopy. The presence of cross peaks between the singlets of the double bond protons (11-H) with the protons of the R^1 substituent and the *ortho* protons of the benzene ring (the numbering of the atoms is different from that accepted by IUPAC) points in favor of structures **6a-c**.

TABLE 1. ^{13}C NMR Spectra (δ, ppm) of Pyrrolothiazolidines **6a-c**, **7a-c**, **8a,d**, and **9a,d**



Thiazo-lidine	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(7)}$	$C_{(8)}$	$C_{(9)}$	$C_{(10)}$	$C_{(11)}$	R^1	R^2	R^3
6a	130.62	116.14	137.17	138.82	159.13	64.30	113.48	113.18	147.90	100.82	27.93 (α-CH_2), 20.74 (β-CH_2), 14.16 (CH_3)	19.40 (CH_2), 14.83 (CH_3)	188.04 (CO) 136.98 (*i*), 127.85 (*o*), 129.13 (*m*), 133.77 (*p*)
7a	132.35	117.56	135.57	138.14	155.02	86.35	164.46	114.36	151.98	100.61	27.94 (α-CH_2), 20.85 (β-CH_2), 14.12 (CH_3)	19.38 (CH_2), 15.06 (CH_3)	188.35 (CO) 136.43 (*i*), 127.80 (*o*), 128.93 (*m*), 133.03 (*p*)
6b	130.57	116.64	135.45	139.45	159.09	64.21	113.48	113.18	147.87	100.85	25.93 (CH_2-1) 29.37 (β-CH_2), 22.99 (CH_2-3), 13.96 (CH_3)	28.13 (CH_2-1), 23.61 (CH_2-2), 13.98 (CH_3)	188.04 (CO) 136.96 (*i*), 127.83 (*o*), 129.10 (*m*), 133.76 (*p*)
7b	132.30	117.53	133.01	138.11	154.96	86.35	164.53	114.87	151.95	100.63	25.92 (α-CH_2), 29.52 (β-CH_2), 22.94 (CH_2-3), 14.04 (CH_3)	28.15 (CH_2-1), 23.77 (CH_2-2), 14.04 (CH_3)	188.35 (CO) 137.03 (*i*), 127.80 (*o*), 128.87 (*m*), 133.81 (*p*)
(*E*)-**8a**	132.22	114.69	129.46	134.87	157.13	56.60	114.56	114.87	124.26	109.36	14.61 (Me-5)	12.25 (Me-4)	31.08 (CH_2S), 15.30 (Me)
(*E*)-**9a**	133.65	112.95	127.63	132.48	153.69	78.39	166.26	118.54	129.28	106.12	14.51 (Me-5)	12.17 (Me-4)	30.91 (CH_2S), 15.26 (Me)
(*Z*)-**8d**	131.43	112.51	131.40	136.43	157.50	60.04	114.10	114.41	135.57	105.00	23.52 (CH_2-4), 22.34 (CH_2-6), 22.34 (CH_2-5), 24.57 (CH_2-7)		30.06 (CH_2S), 15.24 (Me)
(*E*)-**9d**	133.20	112.76	131.27	137.08	157.38	56.77	114.58	114.88	124.30	108.25	23.76 (CH_2-4), 23.03 (CH_2-6) 22.08 (CH_2-5), 26.86 (CH_2-7)		31.10 (CH_2S), 15.31 (Me)



6a–c, 7a–c

The direct coupling constants $^1J_{C(11),H}$ were measured for a more reliable confirmation of the structure of the compounds obtained. The signals in the ^{13}C spectra were assigned using the two-dimensional heteronuclear HMQC and HMBC methods (Table 1). The chemical shifts of the $C_{(11)}$ atom were in the region of 100 ppm, coupling constants $^1J_{C(11),H}$ = 163 Hz, which shows the β-disposition of this atom in relation to the sulfur atom [18].

The reaction is also stereospecific (one isomer) in the case of amide **4b**, although the configuration of the ethenic center has not yet been established successfully. It may only be assumed that the carbamoyl group is turned from the pyrrole ring for steric reasons.

The lower nucleophilicity of the chlorine atom compared with bromine leads to the fact that halogenophilic attack remains less preferred for chloroacetylenes than attack of the *sp*-hybridized carbon atom [13]. Competition for the nucleophile between the halogen and C_{sp} carbon atom in the haloacetylene molecule is illustrated in the example of the reactions of chloro- and bromophenylacetylenes with secondary aliphatic amines in aprotic solvents. The chlorophenylacetylene forms exclusively products of nucleophilic substitution of the chlorine atom with dialkylamines, while under the same conditions phenylacetylene (the product of halogenophilic attack) is obtained from bromophenylacetylene [19]. Among the numerous examples of reactions of organylthiochloroacetylenes, proceeding by a mechanism of nucleophilic substitution of the chlorine atom or the addition of nucleophiles at the multiple bond, with the formation of functionally substituted 1-chloro-2-alkylthioethenes [20], in only one study was halogenophilic attack indicated [21].

The formation of pyrrolothiazolidines **8, 9** from vinylthiolates **2, 3** and acetylene **5b** points against halogenophilic attack since the cyclization of the ethynyl sulfides **12, 13** formed as a result of this attack might also lead to the isomeric thiazine **16, 17**. Probably in the first stage of the process thiolate anions **2, 3** attack the $C_{(\alpha)}$ atom of acetylene **5b**, which leads to chloroethenes **18, 19**. The presence of a strong electron-withdrawing grouping in the α position of the pyrrole ring facilitates ionization of the NH function (by increasing its acidity) which aids the intramolecular cyclization of the intermediates **18, 19** to a mixture of (*E*)- and (*Z*)-pyrrolothiazolidines **8, 9** with different configurations at the double bond. The ratio of isomers is determined both by the structure of the initial pyrrole-2-carbodithioates **1a,d** and by the reaction conditions.

The reaction occurs with the predominant formation of (*E*)-isomers (relative to the double bond formed on cyclization) and with an increase in reaction time their proportion grows. The ratio of the (*E*)- and (*Z*)-isomers of pyrrolothiazolidines **8d** and **9d** formed in 1 h from vinylthiolates **2d, 3d** and acetylene **5b** was 1.2:1 and 2.4:1 respectively, after 2 h for compound **9a** and for compound **9d** it was 4.8:1. After 20 min of the reaction of vinylthiolates **2a, 3a** with acetylene **5b** the ratio of the (*E*)- and (*Z*)-isomers of pyrrolothiazolidines **8a, 8d** was 4.7:1 and 8:1 respectively. However in the process of isolating and purifying (recrystallization from DMSO or elution from aluminum oxide) the (*E*)-isomer is practically completely transformed into the spatially less hindered (*Z*)-isomer. The same conversion is observed when stirring a mixture of isomers in ether in the presence of HCl (shown in the example of thiazolidine **9a**).

A choice between the alternative structures, thiazines **16, 17** and thiazolidines **8, 9** is difficult on the basis of ^{1}H NMR spectra alone. In reality the observed doubling of the signals may be linked with the existence of both (*E*)- and (*Z*)-isomers of pyrrolothiazolidines **8, 9** or a mixture of one of these isomers with thiazines **16, 17**. Reliable confirmation that the synthesized compounds have the structure **8, 9** is obtained with the aid of ^{13}C NMR (Table 1). Assignment of the signals in the ^{13}C NMR spectra was carried out with the aid of two-dimensional HMQC and HMBC heteronuclear methods. The size of the direct coupling constant $^{1}J_{C(11),H}$ (163.3 Hz) in the indicated spectra for a series of compounds enabled an unambiguous choice to be made between structures **8, 9** and **16, 17** [18]. In the HMBC spectra a response was observed of the signal for the protons of the CH_2 group (SEt) at the resonance frequency of the $C_{(11)}$ atom and a response of the 11-H proton signal at the resonance frequency of the methylene carbon atom of the SEt fragment, which also indicates structures **8, 9** where such a correlation is possible.

The determination of the types of isomers for pyrrolothiazolidines **8, 9** was carried out with the aid of a 2D NOESY experiment. In the (*Z*)-isomers there are cross peaks for the signals of the 11-H protons and the substituents at position 5 of the pyrrole ring, which are absent for the (*E*)-isomer. In the ^{1}H NMR spectra the signals of the 11-H protons for the (*Z*)-isomers were displaced towards low field compared with the (*E*)-isomers, which is explained by the ring current of the pyrrole ring. A displacement towards low field was observed for the protons of the 5-Me group in compounds **8a,d** and $C_{(5)}H_2$ in compounds **9a,d** relative to the corresponding signals of the (*E*)-isomers caused by the spatial proximity of the indicated protons to the sulfur atom [22].

Absorption bands for the NH group of the pyrrole ring were absent from the IR spectra of pyrrolothiazolidines **6-9**. The intense bands corresponding to the vibrations of a carbonyl group conjugated with a double bond and a benzene ring in compounds **6, 7** were displayed at 1636-1644 cm^{-1}. Absorption bands for a substituted benzene ring were found at 690-697 cm^{-1} (δ_{C-H}). The C–S bond was displayed at 759-831 and the nitrile group vibration at 2195-2217 cm^{-1}. Bands corresponding to the symmetric and asymmetric vibrations of the amide N–H group in compounds **6-9** were at 3142-3449. The C=O bond of the same group was characterized by the presence of a band in the range 1666-1673 cm^{-1}. The vibrations of the olefinic C=C bond, as well as C=C vibrations of the benzene and pyrrole rings were displayed as series of bands with various intensities in the range 1482-1616 cm^{-1}.

The compounds synthesized were yellow (**8a,d**, **9a,d**) or orange (**6a-c**, **7a-c**) lustrous crystals with high melting points, sparingly soluble in the majority of organic solvents including ether, acetone, acetonitrile, pyridine, carbon disulfide, and DMSO.

EXPERIMENTAL

The IR spectra of the compounds synthesized in the range 400-4000 cm^{-1} were taken in KBr disks on a Bruker IFS 25 Fourier spectrometer. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX 250 spectrometer (250.1 and 62.9 MHz respectively), solvent was $CDCl_3$, and internal standard HMDS. Standard procedures were used for drawing the NOESY and COSY two-dimensional spectra [23,24]. The blending time was selected for each sample and was from 1 to 1.4 sec. The HMQC heteronuclear two-dimensional NMR spectroscopy procedure was used to assign the signals of the carbon atoms in the aromatic fragments of compounds **6-9** [25] and the HMBC procedure was used for the signals of the quaternary carbon atoms [26]. A check on the progress of reactions and the purity of the compounds obtained was carried out by TLC on Silufol UV 254 plates, eluent was diethyl ether. The initial pyrrole-2-carbodithioates **1a-d** were obtained from the corresponding pyrroles and carbon disulfide [27]. 2-Benzoyl-1-bromo- (**5a**), 1-chloro-2-alkylthioacetylenes (**5b**), and 2-(1-iodo-2-propynoxy)-1-methoxyethane (**5c**) were synthesized by the procedures of [28-30] respectively.

Interaction of Pyrrole-2-carbodithioates 1 with CH-acids and Haloacetylenes 5 (Typical Procedure). A suspension of CH-acid **4** (3 mmol) and KOH (3 mmol) in DMSO (20 ml) was stirred at room temperature for 0.5 h, the pyrrole-2-carbodithioate **1** (2 mmol) was then added to it. The mixture was maintained at 108-110°C for 1.5 h, then cooled to room temperature, and haloacetylene **5** (2 mmol) added. The reaction mixture was left for 2 h (in the synthesis of **6a-c**, **7a-c**), 20 min (for **8a-d**), or 1 h (for **9a,d**), and diluted with water (1:3). The precipitated crystals of product were filtered off, washed with water, and recrystallized from DMSO.

2-(3-Benzoylmethylene-6-ethyl-5-propyl-1H-pyrrolo[1,2-*c*]thiazol-1-ylidene)malononitrile (6b). Yield 59%; mp 202°C. IR spectrum, ν, cm^{-1}: 544, 575, 604, 649, 695, 766, 838, 885, 919, 1021, 1039, 1079, 1177, 1221, 1245, 1277, 1291, 1310, 1326, 1380, 1446, 1472, 1523, 1537, 1573, 1594, 1628, 1643, 2209, 2870, 2925, 2953. ^{1}H NMR spectrum, δ, ppm, *J* (Hz): 7.90 (2H, m, *o*-H_{Ph}); 7.61 (1H, m, *p*-H_{Ph}); 7.50 (2H, m, *m*-H_{Ph}); 7.35 (1H, s, 11-H); 7.21 (1H, s, 3-H); 2.95 (2H, t, ^3J = 8.2, α-CH_2 in Pr); 2.50 (2H, q, ^3J = 7.4, CH_2 in Et); 1.78 (2H, m, β-CH_2 in Pr); 1.21 (3H, t, ^3J = 7.4, CH_3 in Et); 1.12 (3H, t, ^3J = 7.2, CH_3 in Pr). Found, %: C 70.45; H 5.07; N 11.48; S 8.29. $C_{22}H_{19}N_3OS$. Calculated, %: C 70.75; H 5.13; N 11.25; S 8.59.

2-(3-Benzoylmethylene-6-ethyl-5-propyl-1H-pyrrolo[1,2-*c*]thiazol-1-ylidene)cyanoacetamide (7b). Yield 63%; mp 260°C. IR spectrum, ν, cm^{-1}: 420, 458, 546, 573, 650, 690, 761, 828, 881, 917, 958, 1024, 1041, 1074, 1156, 1179, 1221, 1246, 1280, 1292, 1312, 1339, 1375, 1393, 1484, 1525, 1540, 1571, 1596, 1616, 1639, 1666, 2194, 2868, 2929, 2953, 3162, 3352. ^{1}H NMR spectrum, δ, ppm, *J* (Hz): 7.90 (2H, m, *o*-H_{Ph}); 7.62 (1H, m, *p*-H_{Ph}); 7.50 (2H, m, *m*-H_{Ph}); 7.35 (1H, s, 11-H); 7.23 (1H, s, 3-H); 6.10 (1H, br. s, $CONH_2$); 5.80 (1H, br. s, $CONH_2$); 2.95 (2H, t, ^3J = 8.2, α-CH_2 in Pr); 2.52 (2H, q, ^3J = 7.4, CH_2 in Et); 1.80 (2H, m, β-CH_2 in Pr); 1.25 (3H, t, ^3J = 7.4, CH_3 in Et); 1.15 (3H, t, ^3J = 7.2, CH_3 in Pr). Found, %: C 67.84; H 5.19; N 10.48; S 8.65. $C_{22}H_{21}N_3O_2S$. Calculated, %: C 67.50; H 5.41; N 10.73; S 8.19.

2-(3-Benzoylmethylene-5-butyl-6-propyl-1H-pyrrolo[1,2-*c*]thiazol-1-ylidene)malononitrile (6c). Yield 65%; mp 196°C. IR spectrum, ν, cm^{-1}: 443, 547, 601, 615, 664, 690, 739, 761, 807, 833, 915, 1024, 1042, 1082, 1120, 1181, 1220, 1244, 1291, 1306, 1320, 1379, 1461, 1482, 1526, 1548, 1575, 1588, 1615, 1644, 2209, 2870, 2928, 2956, 3129. ^{1}H NMR spectrum, δ, ppm, *J* (Hz): 7.94 (2H, m, *o*-H_{Ph}); 7.63 (1H, m, *p*-H_{Ph}); 7.53 (2H, m, *m*-H_{Ph}); 7.38 (1H, s, 11-H); 7.22 (1H, s, 3-H); 2.98 (2H, m, α-CH_2 in Bu); 2.45 (2H, m, α-CH_2 in Pr); 1.72 (2H, m, β-CH_2 in Bu); 1.62 (2H, m, β-CH_2 in Pr); 1.55 (2H, m, γ-CH_2 in Bu); 1.03 (3H, t, ^3J = 7.2, CH_3 in Bu); 0.98 (3H, t, ^3J = 7.3, CH_3 in Pr). Found, %: C 71.44; H 5.41; N 10.38; S 7.85. $C_{24}H_{23}N_3OS$. Calculated, %: C 71.79; H 5.77; N 10.47; S 7.99.

2-(3-Benzoylmethylene-5-butyl-6-propyl-1H-pyrrolo[1,2-*c*]thiazol-1-ylidene)cyanoacetamide (7c). Yield 85%; mp 244°C. IR spectrum, ν, cm^{-1}: 411, 472, 524, 558, 631, 658, 694, 765, 825, 914, 1023, 1041, 1076, 1158, 1178, 1230, 1293, 1336, 1373, 1395, 1486, 1518, 1539, 1572, 1597, 1638, 1673, 2203, 2868, 2928, 2956, 3240, 3302, 3340. ^{1}H NMR spectrum, δ, ppm, *J* (Hz): 7.93 (2H, m, *o*-H_{Ph}); 7.57 (1H, m, *p*-H_{Ph}); 7.48 (2H, m, *m*-H_{Ph}); 7.30 (1H, s, 11-H); 7.20 (1H, s, 3-H); 6.10 (1H, br. s, $CONH_2$); 5.70 (1H, br. s, $CONH_2$); 2.95 (2H, m, α-CH_2 in Bu); 2.45 (2H, m, α-CH_2 in Pr); 1.72 (2H, m, β-CH_2 in Bu); 1.60 (2H, m, β-CH_2 in Pr); 1.55 (2H, m, γ-CH_2 in Bu); 1.03 (3H, t, ^3J = 7.2, CH_3 in Bu); 0.98 (3H, t, ^3J = 7.3, CH_3 in Pr). Found, %: C 68.94; H 6.07; N 10.39; S 7.35. $C_{24}H_{25}N_3O_2S$. Calculated, %: C 68.71; H 6.01; N 10.02; S 7.64.

2-(3-Benzoylmethylene-5,6,7,8-tetrahydrothiazolo[3,4-*a*]indol-1-ylidene)malononitrile (6d). Yield 67%; mp 265°C. IR spectrum, ν, cm^{-1}: 539, 621, 637, 672, 697, 771, 813, 836, 884, 906, 937, 999, 1019, 1041, 1071, 1113, 1143, 1182, 1206, 1225, 1291, 1308, 1343, 1451, 1480, 1523, 1546, 1575, 1595, 1629, 1642, 2217, 2936. ^{1}H NMR spectrum, δ, ppm: 7.95 (2H, m, *o*-H_{Ph}); 7.62 (1H, m, *p*-H_{Ph}); 7.52 (2H, m, *m*-H_{Ph}); 7.36 (1H, s, 11-H); 7.16 (1H, s, 3-H); 3.05 (2H, m, $C_{(5)}$-CH_2); 2.63 (2H, m, $C_{(4)}$-CH_2); 2.03 (2H, m, $C_{(5)}$-CH_2-$\underline{CH_2}$); 1.84 (2H, m, $C_{(4)}$-CH_2-$\underline{CH_2}$). Found, %: C 70.13; H 4.07; N 11.48; S 8.35. $C_{21}H_{15}N_3OS$. Calculated, %: C 70.57; H 4.23; N 11.76; S 8.97.

2-(3-Benzoylmethylene-5,6,7,8-tetrahydrothiazolo[3,4-*a*]indol-1-ylidene)acetamide (7d). Yield 84%; mp 292°C. IR spectrum, ν, cm^{-1}: 473, 485, 505, 530, 551, 574, 617, 636, 679, 691, 740, 759, 815, 838, 872, 905, 940, 1018, 1044, 1136, 1181, 1223, 1263, 1291, 1304, 1349, 1375, 1395, 1444, 1482, 1519, 1542, 1580, 1596, 1637, 1668, 2199, 2946, 3142, 3277, 3300, 3328, 3445. ^{1}H NMR spectrum, δ, ppm: 7.95 (2H, m, *o*-H_{Ph}); 7.55 (1H, m, *p*-H_{Ph}); 7.50 (2H, m, *m*-H_{Ph}); 7.28 (1H, s, 11-H); 7.13 (1H, s, 3-H); 6.00 (1H, br. s, $CONH_2$); 5.50 (1H, br. s, $CONH_2$); 3.00 (2H, m, $C_{(5)}$-CH_2); 2.58 (2H, m, $C_{(4)}$-CH_2); 1.95 (2H, m, $C_{(5)}$-CH_2-$\underline{CH_2}$); 1.78 (2h, m, $C_{(4)}$-CH_2-$\underline{CH_2}$). Found, %: C 66.94; H 4.41; N 11.48; S 8.35. $C_{21}H_{17}N_3O_2S$. Calculated, %: C 67.20; H 4.53; N 11.20; S 8.53.

2-(3-Ethylthiomethylene-5,6-dimethyl-1H-pyrrolo[1,2-*c*]thiazol-1-ylidene)malononitrile (8a). Yield 42%; mp 160°C, (*E*):(*Z*) = 4.7:1, after recrystallization from DMSO (*E*):(*Z*) = 2:1; mp 174-178°C. IR spectrum of isomer mixture, ν, cm^{-1}: 447, 601, 627, 670, 757, 790, 813, 830, 963, 984, 1090, 1110, 1186, 1208, 1245, 1264, 1300, 1326, 1345, 1379, 1449, 1474, 1511 (v s), 1567 (s), 2210, 2862, 2924, 2966, 3025, 3057. ^{1}H NMR spectrum, δ, ppm, *J* (Hz), (*E*)-isomer: 7.05 (1H, s, 3-H); 5.71 (1H, s, 11-H); 2.82 (2H, q, ^3J = 7.5, SCH_2); 2.59 (3H, s, 5-Me); 2.04 (3H, s, 4-Me); 1.32 (3H, t, ^3J = 7.5, Me); (*Z*)-isomer: 7.30 (1H, s, 3-H); 6.36 (1H, s, 11-H); 2.78 (2H, q, ^3J = 7.5, SCH_2); 2.40 (3H, s, 5-Me); 2.07 (3H, s, 4-Me); 1.29 (3H, t, ^3J = 7.5, Me). Found, %: C 58.24; H 4.47; N 14.48; S 22.05. $C_{14}H_{13}N_3S_2$. Calculated, %: C 58.51; H 4.56; N 14.62; S 22.31.

2-(3-Ethylthiomethylene-5,6-dimethyl-1H-pyrrolo[1,2-*c*]thiazol-1-ylidene)cyanoacetamide (9a). Yield 37%; mp 260°C. (*E*):(*Z*) = 8:1. IR spectrum of isomer mixture, ν, cm^{-1}: 449, 496, 539, 577, 624, 645, 759, 811, 831, 961, 980, 1053, 1091, 1138, 1189, 1257, 1290, 1322, 1350, 1380, 1396, 1506, 1568, 1591, 1605, 1653, 2202, 2862, 3193, 3329, 3394. ^{1}H NMR spectrum, δ, ppm, *J* (Hz), (*E*)-isomer: 7.11 (1H, s, 3-H); 5.69 (2H, br. s, $CONH_2$); 5.66 (1H, s, 11-H); 2.81 (2H, q, ^3J = 7.4, CH_2S); 2.63 (3H, s, 5-Me); 2.07 (3H, 4-Me); 1.33 (3H, t, ^3J = 7.4, Me); (*Z*)-isomer: 7.06 (1H, s, 3-H); 6.32 (1H, s, 11-H); 5.69 (2H, br. s, $CONH_2$); 2.78 (2H, q, ^3J = 7.4, CH_2S); 2.40 (3H, s, 5-Me); 2.09 (3H, s, 4-Me); 1.33 (3H, t, ^3J = 7.4, Me). Found, %: C 55.24; H 4.87; N 14.00; S 20.65. $C_{14}H_{15}N_3OS_2$. Calculated, %: C 55.06; H 4.95; N 13.76; S 21.00.

2-(3-Ethylthiomethylene-5,6,7,8-tetrahydro-1H-thiazolo[3,4-*a*]indol-1-ylidene)malononitrile (8d). Yield 68%; mp 160°C, (*E*):(*Z*) = 1.2:1. After recrystallization from DMSO the (*E*)-isomer (purity 95%) was obtained; mp 195-196°C. IR spectrum of isomer mixture, ν, cm^{-1}: 670, 766, 802, 832, 966, 1024, 1059, 1074, 1109, 1147, 1171, 1189, 1208, 1241, 1264, 1289, 1314, 1339, 1364, 1454, 1473, 1518 (v s), 1566 (s), 1587, 2212, 2848, 2932, 3022, 3052. ^{1}H NMR spectrum, δ, ppm, *J* (Hz), (*E*) isomer: 7.07 (1H, s, 3-H); 5.68 (1H, s, 11-H); 3.22 (2H, m, $C_{(5)}$-CH_2); 2.86 (2H, q, ^3J = 7.4, CH_2S); 2.60 (2H, m, $C_{(4)}$-CH_2); 1.78 (4H, m, $C_{(4)}$-CH_2-$\underline{CH_2}$, $C_{(5)}$-$CH_2\underline{CH_2}$); 1.37 (3H, t, ^3J = 7.4, Me); (*Z*) isomer: 7.02 (1H, s, 3-H); 6.33 (1H, s, 11-H); 2.82 (2H, s, $C_{(5)}$-CH_2); 2.80 (2H, q, ^3J = 7.4, CH_2S); 2.60 (2H, m, $C_{(4)}$-CH_2); 1.93 (2H, m, $C_{(5)}$-CH_2-$\underline{CH_2}$); 1.78 (2H, m, $C_{(4)}$-$CH_2\underline{CH_2}$); 1.34 (3H, t, ^3J = 7.4, Me). Found, %: C 60.94; H 4.57; N 13.68; S 20.45. $C_{16}H_{15}N_3S_2$. Calculated, %: C 61.31; H 4.82; N 13.41; S 20.46.

2-(3-Ethylthiomethylene-5,6,7,8-tetrahydro-1H-thiazolo[3,4-*a*]indol-1-ylidene)cyanoacetamide (9d). Yield 67%; mp 222°C. (*E*):(*Z*) = 2.4:1. The (*E*)-isomer (90% purity) was isolated by fractionation on a column of alumina; mp 243-244°C. IR spectrum of the mixture of isomers, ν, cm^{-1}: 607, 619, 648, 668, 732, 761, 806, 832, 952, 1015, 1080, 1136, 1149, 1189, 1257, 1278, 1311, 1336, 1359, 1393, 1451, 1462, 1502 (v s), 1564, 1589, 1611, 1661 (v s), 2207, 2847, 2924, 2977, 3202, 3284, 3342, 3350. ^{1}H NMR spectrum, δ, ppm, *J* (Hz), (*E*)-isomer: 7.08 (1H, s, 3-H); 5.75 (2H, br. s, $CONH_2$); 5.60 (1H, s, 11-H); 3.22 (2H, m, $C_{(5)}$-CH_2); 2.79 (2H, q, ^3J = 7.4, CH_2S); 2.59 (2H, m, $C_{(4)}$-CH_2); 1.77 (4H, m, $C_{(4)}$-CH_2-$\underline{CH_2}$, $C_{(5)}$-CH_2-$\underline{CH_2}$); 1.33 (3H, t, ^3J = 7.4, Me); (*Z*) isomer: 7.03 (1H, s, 3-H); 6.24 (1H, s, 11-H); 5.75 (2H, br. s, $CONH_2$); 2.79 (2H, m, $C_{(5)}$-CH_2); 2.76 (2H, q, ^3J = 7.4, CH_2S); 2.60 (2H, m, $C_{(4)}$-CH_2); 1.89 (2H, m, $C_{(5)}$-CH_2-$\underline{CH_2}$); 1.77 (2H, m, $C_{(4)}$-CH_2-$\underline{CH_2}$); 1.31 (3H, t, ^3J = 7.4, Me). Found, %: C 57.74; H 4.97; N 12.78; S 19.45. $C_{16}H_{17}N_3OS_2$. Calculated, %: C 57.98; H 5.17; N 12.68; S 19.35.

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